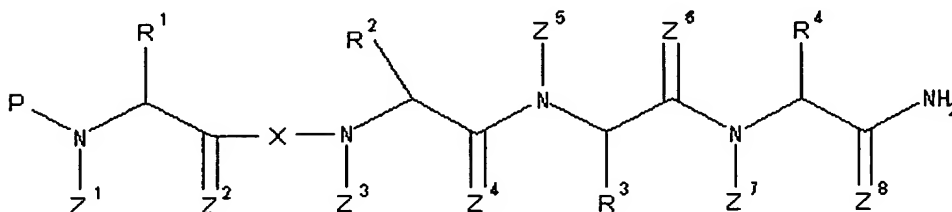


ABSTRACT

The present invention provides a metastatin derivative having excellent blood stability and exhibiting cancer metastasis inhibiting action or cancer growth inhibiting action. Specifically, the present invention the metastatin derivative (I), which is

5 represented by formula:



[wherein, Z^1 , Z^3 , Z^5 and Z^7 represent H or a C_{1-3} alkyl group; Z^2 , Z^4 , Z^6 and Z^8 represent H, O or S; R^1 represents (1) H, or (2) a C_{1-8} alkyl group optionally substituted with a substituent selected from the group consisting of a carbamoyl group, a hydroxyl group and a aromatic cyclic group; R^2 represents (1) H or (2) a cyclic or linear C_{1-10} alkyl group, or (3) a C_{1-10} alkyl group consisting of a cyclic alkyl group and a linear alkyl group; R^3 represents a C_{1-8} alkyl group having a basic group, an aralkyl group having a basic group, a C_{1-4} alkyl group having a non-aromatic cyclic hydrocarbon group of carbon atoms not greater than 7 having a basic group, or a C_{1-4} alkyl group having a non-aromatic heterocyclic group of carbon atoms not greater than 7 having a basic group; R^4 represents a C_{1-4} alkyl group, which may optionally be substituted with a substituent selected from the group consisting of a C_{6-12} aromatic hydrocarbon group, an aromatic heterocyclic group, a C_{8-14} aromatic fused-ring group, an aromatic fused heterocyclic group, a non-aromatic cyclic hydrocarbon group, and a non-aromatic heterocyclic group having carbon atoms not greater than 7; X represents a group shown by formula: $-NHCH(Q^1)YQ^2C(=Z^9)-$ (wherein, Q^1 represents a C_{1-4} alkyl group, which may optionally be substituted with a substituent selected from the group consisting of an aromatic hydrocarbon group, an aromatic heterocyclic group, a C_{8-14} aromatic fused-ring group, an aromatic fused heterocyclic group, a non-aromatic cyclic hydrocarbon group having carbon atoms not greater than 7, and a non-aromatic heterocyclic group having carbon atoms not greater than 7; Q^2 represents CH_2 , NH or O; Y represents $-CONH-$, $-CSNH-$, $-CH_2NH-$, $-NHCO-$, $-CH_2O-$, $-CH_2S-$ or $-CH_2CH_2-$; Z^9 represents H, O or S); and P represents (1) H; (2) an optional amino acid residue

continuously or discontinuously bound from the C-terminal end of the 1-48 amino acid sequence in the amino acid sequence represented by SEQ ID NO: 1; (3) a group represented by formula: $J^1-J^2-C(J^3)(Q^3)Y^1C(J^4)(Q^4)Y^2C(J^5)(Q^5)Y^3C(J^6)(Q^6)C(=Z^{10})-$ (wherein, J^1 represents (a) H or (b) (i) a C_{1-15} acyl group, (ii) a C_{1-15} alkyl group, (iii) a carbamoyl group, (iv) a C_{1-15} alkylcarbamoyl group, (v) a C_{1-15} alkanoylcarbamoyl group, (vi) an aminocarbamoyl group, (vii) a C_{1-15} alkylaminocarbamoyl group, (viii) an oxycarbonyl group, (ix) a C_{1-15} alkoxycarbonyl group, (x) a sulfonyl group, (xi) an amidino group, (xii) a C_{1-15} alkylamidino group, (xiii) a C_{1-15} acylamidino group, (xiv) a C_{1-15} alkylsulfonyl group, or (xv) a oxaryl group, which group may optionally be substituted with cyclic group; J^2 represents NH, CH_2 , O or S; J^3 through J^6 represent H or a C_{1-3} alkyl group; Q^3 through Q^6 represent a C_{1-4} alkyl group, which may optionally be substituted with a substituent selected from the group consisting of a C_{6-12} aromatic hydrocarbon group, an aromatic heterocyclic group, a C_{8-14} aromatic fused-ring group, an aromatic fused heterocyclic group, a non-aromatic cyclic hydrocarbon group having carbon atoms not greater than 7, a non-aromatic heterocyclic group having carbon atoms not greater than 7, an amino group, a guanidino group, a hydroxyl group, a carboxyl group, a carbamoyl group, and a sulfhydryl group, or H; J^3 and Q^3 , J^4 and Q^4 , J^5 and Q^5 or J^6 and Q^6 may be combined together, or, J^2 and Q^3 , Y^1 and Q^4 , Y^2 and Q^5 , or Y^3 and Q^6 may be combined together, to form a ring; Y^1 through Y^3 represent a group represented by formula: $-CON(J^{13})-$, $-CSN(J^{13})-$, $-C(J^{14})N(J^{13})-$ or $-N(J^{13})CO-$ (wherein J^{13} and J^{14} represent H or a C_{1-3} alkyl group); and Z^{10} represents H, O or S); (4) a group represented by formula: $J^1-J^2-C(J^7)(Q^7)Y^2C(J^8)(Q^8)Y^3C(J^9)(Q^9)C(=Z^{10})-$ (wherein, J^1 and J^2 have the same significance as described above; J^7 through J^9 have the same significance as J^3 ; Q^7 through Q^9 have the same significance as Q^3 ; Y^2 and Y^3 have the same significance as described above; Z^{10} has the same significance as described above; J^7 and Q^7 , J^8 and Q^8 or J^9 and Q^9 may be combined together, or, J^2 and Q^7 , Y^2 and Q^8 or Y^3 and Q^9 may be combined together, to form a ring); (5) a group represented by formula: $J^1-J^2-C(J^{10})(Q^{10})Y^3C(J^{11})(Q^{11})C(=Z^{10})-$ (wherein, J^1 and J^2 have the same significance as described above represents; J^{10} and J^{11} have the same significance as J^3 ; Q^{10} and Q^{11} have the same significance as Q^3 ; Y^3 has the same significance as described above; Z^{10} has the same significance as described above; and J^{10} and Q^{10} or J^{11} and Q^{11} may be combined together, or J^2 and Q^{10} or Y^3 and Q^{11} may be combined together, to form a ring); (6) a group represented by formula:

- $J^1-J^2-C(J^{12})(Q^{12})C(=Z^{10})-$ (wherein, J^1 and J^2 have the same significance as described above; J^{12} has the same significance as J^3 ; Q^{12} has the same significance as Q^3 ; Z^{10} has the same significance as described above; and J^{12} and Q^{12} may be combined together, or J^2 and Q^{12} may be combined together, to form a ring); or (7) a
- 5 group represented by formula: J^1- (wherein, J^1 has the same significance as described above)], or a salt thereof.